REMARKS

In response to the office action dated January 9, 2009, Applicants have amended claim 1 to more particularly point out and distinctly claim the subject matter which they regard as their invention. Support for this amendment can be found, e.g., at page 26, line 25 to page 27, line 7 of the specification. Applicants have also amended claims 2, 3, 5, 8, 10, 20, 25, and 26 in view of the amendment to claim 1. Further, Applicants have amended the title of the application. Finally, Applicants have withdrawn claims 21-24, which are directed to a non-elected species (i.e., species I). The Examiner has withdrawn claims 5-7, 10, 11, and 16-19, which are also directed to non-elected species. Claims 1-4, 8, 9, 12-15, 20, 25, and 26 are presented for examination.

Rejections under 35 U.S.C. §103(a)

The Examiner rejects claims 1-4, 8, 9, 12-15, and 20-26 as being obvious on three grounds, each of which is traversed below.

I

Claims 1-3, 8, 9, 13, 14, and 20 are rejected under 35 U.S.C. §103(a) as being obvious from Nishiguchi et al., U.S. Patent No 6,046,040 ("Nishiguchi I") in view of Huang et al., Adv. Synth. Catal. 343 (6-7), 2001, 675-681 ("Huang") with evidential support from Dai, "Intelligent Macromolecules for Smart Devices" published by Springer 2003, page 90.

Independent claim 1 is discussed first. As amended, claim 1 recites a polymer containing (i) 20 to 80 mol% of (meth)acrylic acid residue; (ii) 0.1 to 50 mol% of a first vinyl monomer residue containing a sugar chain and a linker, in which the sugar chain contains a monosacharride or an oligosaccharide residue and the linker contains a selectively cleavable bond; and (iii) at least a second vinyl monomer residue different from the (meth)acrylic acid residue and the first vinyl monomer residue. Applicants found that by adjusting the percentage of the (meth)acrylic acid residue to 20 to 80 mol% and adjusting the percentage of the first vinyl monomer residue to 0.1 to 50 mol%, the density of sugar chains in the polymer could be controlled so that the polymer thus obtained exhibited a high sugar transfer efficiency when used as a primer during a glycosylation reaction. *See, e.g.*, Table 1 on page 44 of the specification.

Nishiguchi I describes a method for producing a glycoconjugate that includes binding a sugar residue to the side chain of a water-soluble polymer via a linker having a selectively cleavable linkage to give a primer, and bringing the primer into contact with an immobilized glycosyltransferase in the presence of a sugar nucleotide to transfer a sugar residue of the sugar nucleotide to the sugar residue of the primer. *See, e.g.*, the abstract. However, as correctly pointed out by the Examiner, Nishiguchi I does not disclose or render obvious a polymer containing 20 to 80 mol% of (meth)acrylic acid residue, as recited by amended claim 1. In addition, Nishiguchi I does not disclose or render obvious a polymer containing three different monomer residues (i.e., the (meth)acrylic acid residue, the first vinyl monomer residue, and the second vinyl monomer residue) and 0.1 to 50 mol% of the first vinyl monomer residue, as recited by amended claim 1.

It would not have been obvious to combine Huang with Nishiguchi I to provide the polymer recited in amended claim 1. The Examiner asserts that

> "The thermo-responsive polymer [described in Huang] comprises N-isopropylacrylamide, acrylic acid, with or without N-tert-butylacrylamine (Figure 1 on page 676). ... All things being equal, an increase in the content of acrylic acid in a copolymer tends to increase the LCST [i.e., lower critical solution temperature] of the copolymer as shown in polymers A and B (Figure 1, page 676)." *See* the office action, the paragraph bridging pages 3 and 4.

The Examiner clearly errs. Huang describes immobilizing enzymes on a thermo-responsive support polymer. *See, e.g.*, the abstract. However, Huang describes in Figure 1 on page 676 a thermo-responsive support polymer containing N-isopropylacrylamide (NIPAM), N-t-butylacrylamide (NTBAM), and N-acrylylsuccinamide (NASI), not a polymer containing acrylic acid as asserted by the Examiner. Thus, given that Huang discusses the LCST of a polymer that does not contain acrylic acid, Huang does not disclose or render obvious that an increase in the content of acrylic acid in a copolymer would increase the LCST of the copolymer.

The Examiner also asserts that "the followings are taught [in Huang]: ... (B) if the polymer is soluble during the glycosylation, the composition of the polymer can be manipulated to change its LCST so as to (a) increase the efficiency of the glycosylation and (b) enhancing facile isolation of the products as well as facilitate the recyclability of the catalytic system (p. 676)." *Id.* However, Huang describes the relationship between the LCST of a support polymer

and the enzymatic activity of an enzyme-polymer adduct prepared from the support polymer (i.e., corresponding to the immobilized glycosyltransferase described in Nishiguchi I), not the relationship between the LCST of a support polymer and the activity of a primer for glycoconjugate synthesis (which includes a sugar residue, not an enzyme, on the support polymer) taught in Nishiguchi I. It would have been apparent to one skilled in the art that the enzymatic activity of an immobilized glycosyltransferase is significantly different from the activity of a primer for glycocojugate synthesis. In addition, although Huang describes a primer for glycoconjugate synthesis, it does not disclose any relationship between the activity of the primer and the LCST of the support polymer or the amount of acrylic acid in the support polymer.

In sum, Huang does not teach any relationship between the LCST of a support polymer and the amount of acrylic acid in the support polymer. Nor does Huang teach any relationship between the LCST of a support polymer and the activity of a primer for glycoconjugate synthesis, such as the polymer recited in amended claim 1. Thus, it would not have been obvious for one skilled in the art to combine Huang and Nishiguchi I to provide the polymer recited in amended claim 1.

Dai does not cure the deficiencies in Huang and Nishiguchi I. The Examiner asserts that

> "It is well known in the art that in a thermo-responsive copolymer such as random copolymer of N-isopropylacrylamide (NIPAM) and acrylic acid (AA), increasing the content of the acrylic acid will increase the LCST of the copolymer. (See, Dai, page 90). Thus, if an intended enzymatic reaction is done at, say 37°C, a copolymer of NIPAM and AA having less than 20 mol% AA would have LCST lower than 37°C (i.e., it is insoluble at that temperature) and it is therefore not beneficial to the [glycosylation] reaction." *See* the office action, page 4, 2nd paragraph.

However, Dai only describes that a copolymer of NIPAM and AA having less than 20 mol% of AA would have a LCST lower than 37°C at a pH of 4. By contrast, the polymer recited in amended claim 1 is generally used as a primer in glycoconjugate synthesis, which is typically conducted at a pH from about 7 to 7.5. *See, e.g.*, Example 10 of the present application and the subsection entitled "Buffers, Enzymes, and Sugar Necleotide used for each Glycosylation" in the experimental section in Huang. Dai describes in Figure 3.7 that, at this pH range (i.e., at a pH of

7.4), the LCST of the NIPAM-AA copolymer containing 7 wt% (i.e., 10.6 mol%) of AA is higher than 60°C, which is significantly higher than 37°C. In other words, Dai suggests that a NIPAM-AA copolymer containing 10.6 mol% of AA or more would be soluble at 37°C at pH 7.4.[1] Thus, contrary to the Examiner's assertion, Dai teaches that a NIPAM-AA copolymer having 10.6 mol% (which is less than 20 mol%) of AA is soluble in water at 37°C at pH 7.4. It follows that it would not have been obvious for one skilled in the art to increase the percentage of AA in a copolymer from 10.6 mol% to 20 mol% to provide a polymer of amended claim 1 for use as a primer for glycoconjugate synthesis (which is typically conducted at pH about 7 to 7.5).

For the reasons set forth above, it would not have been obvious to combine Nishiguchi I with Huang and Dai to provide the polymer recited in amended claim 1. Thus, claim 1 would not have been obvious from Nishiguchi I in view of Huang and Dai. As claims 2, 3, 8, 9, 13, 14, and 20 depend from claim 1, they also would not have been obvious from Nishiguchi I in view of Huang and Dai.

II

Claims 1-3, 12-15, and 20 are rejected under 35 U.S.C. §103(a) as being obvious from Nishiguchi et al., JP 2001-220399 ("Nishiguchi II") in view of Huang with evidential support from Dai.

Independent claim 1 is discussed first. As discussed above, amended claim 1 recites a polymer containing (i) 20 to 80 mol% of (meth)acrylic acid residue; (ii) 0.1 to 50 mol% of a first vinyl monomer residue containing a sugar chain and a linker, in which the sugar chain contains a monosacharride or an oligosaccharide residue and the linker contains a selectively cleavable bond; and (iii) at least a second vinyl monomer residue different from the (meth)acrylic acid residue and the first vinyl monomer residue.

Nishiguchi II describes glycopeptides that can include monosaccharide residues. *See, e.g.*, claim 1. Like Nishiguchi I, Nishiguchi II does not disclose or render obvious a polymer containing three different monomer residues (i.e., the (meth)acrylic acid residue, the first vinyl monomer residue, and the second monomer residue), which include 20 to 80 mol% of the

[1] Dai describes that a NIPA-AA copolymer tends to have a higher LCST when it contains more AA (*see* Figure 3.7) and Huang describes that a thermo-responsive water-soluble polymer would be soluble in water when the water temperature is lower than the LCST of the polymer (*see* the introduction).

(meth)acrylic acid residue and 0.1 to 50 mol% of the first vinyl monomer residue, as recited by amended claim 1.

As discussed above, Huang does not teach any relationship between the LCST of a support polymer and the amount of acrylic acid in the support polymer. Nor does Huang teach any relationship between the LCST of a support polymer and the activity of a primer for glycoconjugate synthesis, such as the polymer recited in amended claim 1. As also discussed above, Dai does not cure the deficiencies in Huang. Thus, it would not have been obvious to combine Nishiguchi II with Huang and Dai to provide the polymer recited in amended claim 1.

Thus, claim 1 would not have been obvious from Nishiguchi II in view of Huang and Dai. As claims 2, 3, 12-15, and 20 depend from claim 1, they also would not have been obvious from Nishiguchi II in view of Huang and Dai.

III

Claims 1-4, 8, 9, 13, 14, and 20-26 are rejected under 35 U.S.C. §103(a) as being obvious from Yamada et al., Carbohydrate Research 305 (1998), 443-461 ("Yamada") in view of Huang with evidential support from Dalkas et al., Polymer 47 (2006) 243-248.

Independent claim 1 is discussed first. As discussed above, amended claim 1 recites a polymer containing (i) 20 to 80 mol% of (meth)acrylic acid residue; (ii) 0.1 to 50 mol% of a first vinyl monomer residue containing a sugar chain and a linker, in which the sugar chain contains a monosacharride or an oligosaccharide residue and the linker contains a selectively cleavable bond; and (iii) at least a second vinyl monomer residue different from the (meth)acrylic acid residue and the first vinyl monomer residue.

Yamada describes copolymerizing glycomonomers (which includes sugar residues) with acrylamide to give glycopolymers, which can be used in sugar elongation reaction in the presence of a glycosyl transferase. *See, e.g.*, the abstract. Like Nishiguchi I and II, Yamada does not disclose or render obvious a polymer containing three different monomer residues (i.e., the (meth)acrylic acid residue, the first vinyl monomer residue, and the second monomer residue), which include 20 to 80 mol% of the (meth)acrylic acid residue and 0.1 to 50 mol% of the first vinyl monomer residue, as recited in amended claim 1.

As discussed above, Huang does not teach any relationship between the LCST of a support polymer and the amount of acrylic acid in the support polymer. Nor does Huang teach any relationship between the LCST of a support polymer and the activity of a primer for glycoconjugate synthesis, such as the polymer recited in amended claim 1. Thus, it would not have been obvious to combine Yamada with Huang to provide the polymer recited in amended claim 1.

The Examiner relies on Dalkas to show that homopolymer of acrylamide (a comonomer used in Yamada) is highly soluble in water and is therefore not thermo-responsive. The Examiner then proceeds to conclude that use of only acrylamide in Yamada's glycopolymers does not work toward facilitating efficient separation of the products from the reactants because the separation cannot be achieved simply by changing the temperature to precipitate either the products or the reactants. *See* the office action, page 8, 2nd paragraph. However, Yamada discloses that its products (i.e., glycoconjugates) can be obtained in high yield by cleaving the linker between the support polymer and the sugar residues. In other words, it would have been apparent to one skilled in the art that it is unnecessary for Yamada's glycopolymers to be thermo-responsive to facilitate separation of Yamada's products. Thus, it would not have been obvious to insert acrylic acid residues into the glycopolymers described in Yamada to adjust the solubility of the glycopolymers.

Thus, claim 1 would not have been obvious from Yamada in view of Huang and Dalkas. As claims 2-4, 8, 9, 13, 14, 25, and 26 depend from claim 1, they also would not have been obvious from Yamada in view of Huang and Dalkas.

CONCLUSION

Applicants submit that the grounds for rejection asserted by the Examiner have been overcome and that all pending claims are now in condition for allowance, which action is requested.

Any circumstance in which Applicants have: (a) addressed certain comments of the Examiner does not mean that Applicants concede other comments of the Examiner; (b) made arguments for the patentability of some claims does not mean that there are not other good reasons for the patentability of those claims and other claims; or (c) amended or canceled a claim

does not mean that Applicants concede any of the Examiner's positions with respect to that claim or other claims.

The Petition for One-Month Extension of Time fee in the amount of $130.00 is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges to deposit account 06-1050, referencing Attorney's Docket No. 18900-0003US1.

Respectfully submitted,

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